1) Who uses IRIS? i.e. Who are the clients, e.g. OLEM, OAR, OW, OCSPP and others?

IRIS was created in 1985 to address the confusion and inconsistency that arose previously when different EPA programs conducted separate assessments that resulted in different hazard conclusions or toxicity values for the same chemical. IRIS assessments are the top tier products in the hierarchies used by OLEM, OAR, and OW for using assessments as the basis for their programmatic decisions.

- **OLEM:** OLEM does not conduct its own hazard and dose-response assessments. OLEM relies on IRIS to inform clean-up decisions at contaminated Superfund and hazardous waste sites. IRIS assessments provide toxicity values to inform site-specific cleanups.
- **OAR:** IRIS assessments are key to the Risk and Technology Reviews (RTR) required under the Clean Air Act Title III (there is currently a court-ordered deadline to review 20 source categories in 3 years).
- **OW:** IRIS assessments are used to set health advisories, maximum contaminant levels, and other actions in the Office of Water. OW nominates and prioritizes chemicals for IRIS assessment that are high-profile and more controversial and that would take additional time and resources to complete. They also look to IRIS experts for support on actions based on completed assessments; perchlorate is a recent example. IRIS experts also provide support on high profile chemical activities in the agency - lead and PFAs are recent examples.
- **OCSPP/OPPT:** IRIS staff are currently working in direct support of the first 10 chemical assessments, providing chemical specific expertise for scoping and evaluating health hazard information, quality checks for work completed by contractors, and training and assistance in implementing best practices of systematic review and evidence synthesis. IRIS staff are also helping to develop automated software workflows directed at expediting the pace and throughput of chemical assessments. IRIS is helping OPPT implement efficiencies to meet their TSCA timelines; additionally, IRIS is aiming to shorten NCEA's chemical evaluation timeline to ~2 years (pre- peer review) to be more consistent with TSCA timelines.
- **Other Agencies:** IRIS assessments are important resources for other federal, state, and international agencies. For example, DOD policy instructions for the management of emerging contaminants identify IRIS assessments as the top tier of chemical information to be used in conducting risk assessments for contaminated sites (DODI 4715.18). IRIS experts also frequently provide continual support to risk managers and regulators in support of priority and emergency issues.

2) What are alternatives to IRIS – if yes, what would the timeline look like?

- There are no current alternatives to IRIS. See below for proposed ORD/NCEA alternative.
- There is an expectation that TSCA, modernized under the Lautenberg Act, can replace the functions of IRIS. But TSCA addresses chemicals in commerce.
    - It does NOT support other activities such as site cleanups, drinking water evaluations, etc. IRIS provides these types of support across EPA, and for states and tribal nations.
    - Chemical evaluations under TSCA do not provide the reference values statutorily required by other programs.
    - IRIS also evaluates naturally occurring chemicals (like manganese) and chemical degradants.
- The IRIS Program is a critical resource to EPA and the risk assessment community. The IRIS Program utilizes a multi-step process which provides multiple opportunities for public,

stakeholder, and interagency engagement. The assessments are complex, multidisciplinary evaluations of scientific information, which are developed through a transparent and systematic process with robust, independent peer review. IRIS is the only federal program to provide toxicity values for both cancer and non-cancer effects.

ORD/NCEA Alternative:

- Timely and effective chemical risk assessments to inform public health decisions and provide transparency and certainty to the regulated community have been difficult to produce.
- Input from examiners in OMB/OIRA indicates that federal partners see the IRIS Program and process as a valuable critical approach to provide toxicity values to the federal community. The DOD Instruction on Emerging Contaminants indicates IRIS assessments are first tier toxicity values used in site-specific risk assessments.
- In addition, they strongly recommend that because of its broad and ubiquitous application, IRIS be maintained in ORD and separate from any one risk management or regulatory strategy.
- NCEA has been working on this issue since January 2017 from two perspectives, 1) Maintain the patina and imprimatur of the IRIS Program, but gut and modernize it; or 2) build it from scratch.
- NCEA and ORD are prepared to adopt either approach to rebuilding the program – with or without the IRIS imprimatur -- use existing FTE and resources to build out the program, and demonstrate a transformation in 12-18 months.
- With combined expertise in private sector, federal government, and NGO, new NCEA leadership presents a 'power team' that has the scientific credentials, networks, and credibility to effect this change without a severe backlash to EPA leadership.
    - Tina Bahadori has consulting, EPRI, ACC, and EPA experience, and has served on several NAS Board/committee/working groups.
    - Kris Thayer has NGO and NIH experience
    - Both have deep connections in the academic community

3) What are the consequences of eliminating IRIS? Pros/cons

Pros:

- Strong external support from ACC, API, large manufacturers, SBA, and their advocacy network surrounding Congress. This might provide relief from other pressures.
- Eliminating the IRIS Program but retaining resources and expertise in ORD would provide an opportunity to implement a chemical evaluation portfolio (Attachment 1, below) with maximum flexibility to ensure that products meet Agency needs without the burden of IRIS.

Cons:

- Strong negative reaction from the public health community in academia, NGOs, and some of the states (like California).
- Program and Regional offices will need to do their own assessments for which they don't have expertise, experience, resources, or time.
    - Scattering of toxicity values and risk assessments for same chemicals.
    - TSCA can hardly fulfill its own mandate to evaluate chemicals in commerce. Again, it does NOT support other activities such as site cleanups, drinking water evaluations, evaluation of natural chemicals, such as manganese, etc.
    - Superfund would be handicapped.
- Chemical assessments require multidisciplinary teams with expertise in toxicology,

epidemiology, statistics, risk assessment, exposure assessment, developmental health, pharmacokinetics, etc. IRIS has assembled such expertise – scattering the resources and FTE's across EPA will simply create dysfunction and would not meaningfully increase the assessment development capacity in each program office.

- EPA would revert back to a time before IRIS when there were complaints about lack of transparency and consistency in agency risk assessment/risk management decisions.
    - Externally, some stakeholders would be critical that EPA is not adhering to its public health mandate.

4) What specific info does IRIS provide that the client specifically wants? Does an IRIS assessment provide the same values for each assessment? Why is this information valuable?

IRIS assessments provide 1) an identification of the hazards associated with exposure to a chemical, and 2) toxicity values that quantitatively establish the relationship between exposure to a chemical and hazard (both cancer and non-cancer). IRIS assessments provide these values only when data are sufficient to make a decision. The hazard information and toxicity values provided by IRIS serve as the scientific foundation of risk assessments decisions made across the Agency.

BUT -- IRIS assessments are <u>not</u> risk assessments or regulatory decisions. They are the top tier source of toxicity information used by EPA and other health agencies to inform national standards, clean-up levels at local sites, and set advisory levels. IRIS is the only federal program that provides toxicity values for cancer and non-cancer effects. This information is critical to combine with exposure information in order to make numerous agency decisions.

In other words – IRIS <u>synthesizes</u> the literature/science about hazard/toxicity. Regulatory bodies and risk managers make the decisions and set the standards.

The IRIS Program also has ancillary products and provides significant collateral benefit. IRIS experts provide important support to other Agency activities that require expertise in epidemiology, developmental health, statistics, modeling, etc. – again, perchlorate, lead, PFAs are recent examples.

5) What are all current IRIS assessments that NCEA is working on? Are they being done using the 2011 recommendations?

As provided by the NAS 2011 and 2014 recommendations, the IRIS Program began phasing in and implementing the recommendations for assessments under development. The table below summarizes this information:

Increasing Implementation of NRC Recommendations

IRIS CHEMICAL ASSESSMENTS CURRENTLY IN DEVELOPMENT		IMPLEMENTED NRC 2011 RECOMMENDATIONS
Draft Assessments	Chloroform	✓ Establishes standard chemical-specific systematic review protocols for evidence identification and integration ✓ Comprehensive, systematic literature search and screening approach documented in a table and flow diagram (inclusion/exclusion of studies) ✓ Studies were evaluated uniformly for aspects of design, conduct, or reporting that could affect the interpretation of results and contribution to the synthesis of evidence ✓ Summary evaluation included in the section on methods for identifying and selecting studies ✓ All references web-accessible through EPA's Health and Environmental Research Online (HERO) database ✓ Utilization of new systematic review software tools and practices to advance the presentation of evidence tables, forest plots, and other graphical displays of data ✓ Streamline assessments using tables, figures, and appendices ✓ Distinct sections for literature search and study selection, hazard identification, and dose-response ✓ Evidence is presented in standardized summary and evidence tables and in exposure-response arrays ✓ Strengthened, integrated, and transparent discussion of the weight of available evidence ✓ Incorporation of strength of evidence descriptors for non-cancer effects ✓ Clear rationale or selection and advancement of studies considered for calculating reference values and unit risks ✓ Transparent description of the decisions made in calculation of reference values and unit risks (implemented as appropriate and as science evolves)
	Methylmercury	
	Ammonia (Oral)	
	Manganese	
	Nitrate/Nitrite	
	Ethylbenzene	
	Polychlorinated Biphenyls (PCBs)	
	Phthalates (DIBP, DEP, Multi-Phthalate, DINP, DBP, BBP)	
	Hexavalent Chromium	
	Naphthalene	
	Hexabromocyclododecane (HBCD)	
	Polycyclic Aromatic Hydrocarbons (PAH Mixtures)	
	Inorganic Arsenic	
	Formaldehyde	
Post-Peer Review	RDX	
	Ethyl-Tert-Butyl Ether (ETBE)	
	Tert-Butanol (TBA)	

6) How and who decides on which IRIS assessments NCEA conducts?

The list of potential chemicals is driven by Agency nominations. Nominations are also solicited from other federal agencies, the Executive Office of the President, and the public (including states, industry,

and other stakeholders). Assessments are prioritized according to Agency needs and available capacity/resources within the IRIS Program. The IRIS Multi-Year Agenda, issued in December 2015 and published in the Federal Register, provides an outlook on the planned assessments that were identified and prioritized, and scaled to the projected resources. Starting in 2018, however, the IRIS Program will reconfirm this information annually to ensure that it remains responsive.

IRIS Criteria for Chemical Selection

- Potential public health impact
- EPA statutory, regulatory, or program-specific implementation needs
- Availability of new scientific information or methodology that might significantly change the current IRIS information
- Interest to other governmental agencies or the public
- Availability of other scientific assessment documents that could serve as a basis for development of an IRIS assessment
- Other factors such as widespread exposure

7) In the past, what has been the typical time period for an IRIS assessment?

Assessments in the past took about 3-7 years, depending on complexity. High-profile or controversial chemicals under assessment (for example, formaldehyde and inorganic arsenic) have taken 10 years or more, and had multiple peer reviews. In response to stakeholder requests and congressional inquiries, in 2013, the IRIS process was enhanced to include additional layers of public interactions and extended timelines for peer review, the baseline time to complete an assessment has increased significantly (by almost 50%).

8) Will the new portfolio approach reduce that time period (set an expectation for a timely assessment)

(See Attachment 1, below for more details on the Portfolio approach)
The portfolio approach offers a nimble, flexible and efficient way to draw on new data streams, develop a continuum of risk assessment products, better meet the needs of stakeholders and decision makers. It also significantly increases the speed, transparency and access to assessment products and democratizes the process for all stakeholders impacted by decisions.

It is important to note that there are certain aspects of the IRIS process (for example, sequential agency and interagency review, separate and sequential public comment and peer review drafts, and final agency and interagency review steps) that add to the length of time to complete an assessment. Altering the steps of the IRIS process would help facilitate timely assessments; however, this could result in significant controversy with other federal agencies and industry groups.

9) When will transition to new IRIS happen e.g, after formaldehyde assessment is out the door?

The transition to "new IRIS" is already well underway – please see table in item 5 above. Chemicals under active draft development (i.e., not yet released for intra-agency review) address all the systematic review recommendations of the 2014 NAS report. In 2017 staff have been trained on use of computational and specialized software applications designed to enhance the transparency and accelerate the pace of conducting an assessment. These approaches are being implemented for "new starts." In addition, a fit-for-purpose concept of the portfolio is being applied to all new starts.

Assessments currently in draft development are being evaluated to identify opportunities to streamline and speed development times. This transition will become more evident as materials are released for public comment and with discussion at future meetings.

10) Does the formaldehyde assessment follow the recommendations from the 2011 report? If not, why not? Is so, will subsequent assessments follow that same approach?

Yes, the formaldehyde assessment follows the recommendations from the 2011 NRC report. Subsequent assessments will also be consistent with the 2011 NRC report recommendations and more importantly continue to evolve in application of new systematic review methods, as the science progresses. IRIS is coordinating with OCSPP and other EPA partners, through a Community of Practice, to ensure consistent development of these methods.

11) Regarding the portfolio approach, how will these assessments better tailor to meet the needs of decision makers – please use an example, e.g. will provide X values within X months?

See Attachment 1 below for more detail on the Portfolio approach.

In certain cases, the scoping needs may identify a chemical with a small evidence base. For example, updated assessments for a chemical with an existing IRIS value. When the evidence base is relatively small (<50 key studies), the IRIS Program expects to produce a draft assessment within 6-9 months with current staffing. We are training staff on software and project management workflows to implement rapid assessments and will have examples within the next 6 months. In addition, we are positioning staff to be familiar with RapidTox approaches for conducting assessments. A portfolio approach benefits from early and frequent engagement with decision makers to most effectively tailor the assessment to meet the needs. By focusing on the decision-making science, NCEA can be more efficient and timely in assessment development.

12) Is the IRIS handbook ready for public release?

Yes. Note that OMB has requested to review the document prior to public release.

Attachment 1 -- Portfolio Approach to Chemical Risk Assessment

Problem: Timely and effective chemical risk assessments to inform public health decisions and provide transparency and certainty to the regulated community have been difficult to produce.

Background:

- EPA, states, and others use chemical risk assessment as a scientific foundation for decisions about environmental exposures and public health.
- As such, they have significant implications to the protection of environment and public health, as well as to the economy and sustainable development.
- For this reason, as a science, risk assessment is the subject of significant controversy.
- There are currently tens of thousands of chemicals in commerce, and other 'legacy' chemicals, can be found in Superfund sites, and others are emitted from sources in different industries.
- Traditional risk assessments have relied on animal toxicity testing data to inform hazard evaluation – these type of data are available for only a small subset of chemicals (~500).
- More and more human relevant data are being generated through epidemiology, high throughput toxicity testing, and other novel technologies.
- While the new data presents many new possibilities for better risk assessments, the process for scientific consensus on how to use these data is in its infancy and many 'acceptance' barriers have to be overcome.
- TSCA's new mandate for alternatives to animal testing provides exciting new possibilities.
- Many advisory committees (such as the NAS), have provided recommendations for overcoming these barriers and accelerating the pace of chemical risk assessment by:
    - developing ways to use new data from high throughput and other test methods to quickly provide information on chemicals' effects (NRC 2007; NRC 2017);
    - streamlining the lengthy assessment development processes (GAO 2008; GAO 2011);
- In order for risk assessment to meet the current demands to protect the environment and public health without crippling sustainable development, a significant transformation is needed.

Approach/Recommendations: A portfolio approach to risk assessment offers a continuum of products ranging from rapid screening of chemicals to the more complex scientific assessment of a large body of evidence from human and animal studies.

The proposed approach will increase public health protection by:

- moving away from a 'one-size-fits-all' approach to chemical risk assessment towards a spectrum of assessment products to meet specific decision contexts;
- facilitating the incorporation of new science into risk assessment and decision-making;
- enabling assessments to be better tailored to meet needs of decision makers;
- increasing the number of chemicals that can be evaluated for their effects on human health by utilizing constrained resources in the most efficient manner.

Takeaway: This portfolio approach offers a nimble, flexible and efficient way to draw on new data streams, develop a continuum of risk assessment products, better meet the needs of stakeholders and decision makers. It also significantly increases the speed, transparency and access to assessment products and democratizes the process for all stakeholders impacted by decisions.

Opportunity: The approach could be piloted on the PFAS class of chemicals, which differ markedly in the amount of available information assess risks by traditional approaches.